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L1: Entry 1 of 1 File: USPT Feb 18, 2003

US-PAT-NO: 6521746
DOCUMENT-IDENTIFIER: US 6521746 B1

TITLE: Polynucleotides encoding LKT 111

DATE-ISSUED: February 18, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Potter; Andrew A.	Saskatoon			CA
Manns; John G.	Saskatoon			CA

US-CL-CURRENT: 536/23.1; 435/252.3, 435/320.1, 435/455, 435/69.1, 435/69.3, 435/69.7, 536/23.4, 536/23.7

CLAIMS:

What is claimed is:

1. A polynucleotide comprising a coding sequence for an LKT 111 polypeptide, said polynucleotide comprising the contiguous polynucleotide sequence of nucleotides 31 to 1473 of SEQ ID NO:9, or a polynucleotide with at least 80% sequence identity thereto.

2. The polynucleotide of claim 1, wherein the polynucleotide comprises a polynucleotide sequence with at least 90% sequence identity to the contiguous polynucleotide sequence of nucleotides 31 to 1473 of SEQ ID NO:9.

3. The polynucleotide of claim 1, wherein the polynucleotide comprises a polynucleotide sequence with at least 95% sequence identity to the contiguous polynucleotide sequence of nucleotides 31 to 1473 of SEQ ID NO:9.

4. The polynucleotide of claim 1, wherein the polynucleotide comprises the contiguous polynucleotide sequence of nucleotides 31 to 1473 of SEQ ID NO:9.

5. The polynucleotide of claim 1, wherein said polynucleotide comprises a polynucleotide sequence encoding amino acids 11-491 of SEQ ID NO:10.

6. A recombinant vector comprising the polynucleotide of claim 1 and control elements operably linked to said polynucleotide, whereby said coding sequence of said polynucleotide can be transcribed and translated in a host cell.

7. A recombinant vector comprising the polynucleotide of claim 2 and control elements operably linked to said polynucleotide, whereby said coding sequence of said polynucleotide can be transcribed and translated in a host cell.

8. A recombinant vector comprising the polynucleotide of claim 3 and control elements operably linked to said polynucleotide, whereby said coding sequence of said polynucleotide can be transcribed and translated in a host cell.

9. A recombinant vector comprising the polynucleotide of claim 4 and control

elements operably linked to said polynucleotide, whereby said coding sequence of said polynucleotide can be transcribed and translated in a host cell.

10. A recombinant vector comprising the polynucleotide of claim 5 and control elements operably linked to said polynucleotide, whereby said coding sequence of said polynucleotide can be transcribed and translated in a host cell.

11. A host cell transformed with the recombinant vector of claim 6.

12. A host cell transformed with the recombinant vector of claim 7.

13. A host cell transformed with the recombinant vector of claim 8.

14. A host cell transformed with the recombinant vector of claim 9.

15. A host cell transformed with the recombinant vector of claim 10.

16. A method of producing a recombinant polypeptide comprising: (a) providing a population of host cells according to claim 11; and (b) culturing said population of host cells under conditions whereby the polypeptide encoded by said polynucleotide is expressed.

17. A method of producing a recombinant polypeptide comprising: (a) providing a population of host cells according to claim 12; and (b) culturing said population of host cells under conditions whereby the polypeptide encoded by said polynucleotide is expressed.

18. A method of producing a recombinant polypeptide comprising: (a) providing a population of host cells according to claim 13; and (b) culturing said population of host cells under conditions whereby the polypeptide encoded by said polynucleotide is expressed.

19. A method of producing a recombinant polypeptide comprising: (a) providing a population of host cells according to claim 14; and (b) culturing said population of host cells under conditions whereby the polypeptide encoded by said polynucleotide is expressed.

20. A method of producing a recombinant polypeptide comprising: (a) providing a population of host cells according to claim 15; and (b) culturing said population of host cells under conditions whereby the polypeptide encoded by said polynucleotide is expressed.

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L2: Entry 2 of 2 File: USPT Feb 8, 2000

US-PAT-NO: 6022960
DOCUMENT-IDENTIFIER: US 6022960 A

TITLE: GnRH-leukotoxin chimeras

DATE-ISSUED: February 8, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Potter; Andrew A.	Saskatoon			CA
Manns; John G.	Saskatoon			CA

ASSIGNEE-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY	TYPE CODE
University of Saskatchewan	Saskatoon			CA	03

APPL-NO: 09/ 124491 [PALM]
DATE FILED: July 29, 1998

PARENT-CASE:
CROSS-REFERENCE TO RELATED APPLICATION This application is a divisional of U.S. Patent application Ser. No. 08/694,865 filed on Aug. 9, 1996 now U.S. Pat No. 5,837,268 which is a continuation-in-part of U.S. patent application Ser. No. 08/387,156, filed Feb. 10, 1995 now U.S. Pat. No. 5,723,129 which is a continuation-in-part of U.S. patent. application Ser. No. 07/960,932, fled Oct. 14, 1992 (issued as U.S. Pat. No. 5,422,110), which is a continuation-in-part of U.S. patent application Ser. No. 07/779,171 filed Oct. 16, 1991, now abandoned.

INT-CL: [06] C07 H 2/04, C07 H 2/02, C12 P 21/06, A61 K 39/00

US-CL-ISSUED: 536/23.1; 536/23.4, 536/23.7, 424/184.1, 424/235.1, 435/320.1, 435/252.3, 435/69.3, 435/69.7, 435/172.1, 435/172.3
US-CL-CURRENT: 536/23.1; 424/184.1, 424/235.1, 435/252.3, 435/320.1, 435/69.3, 435/69.7, 536/23.4, 536/23.7

FIELD-OF-SEARCH: 424/184.1, 424/235.1, 435/320.1, 435/252.3, 435/69.3, 435/69.7, 435/172.1, 435/172.3, 536/23.1, 536/23.4, 536/23.7

PRIOR-ART-DISCLOSED:

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	PAT-NO	ISSUE-DATE	PATENTEE-NAME	US-CL
☐	4556555	December 1985	Esbenshade	
☐	4608251	August 1986	Mia	
☐	4692412	September 1987	Livingston et al.	
☐	4975420	December 1990	Silversides et al.	
☐	5028423	July 1991	Prickett	
☐	5055400	October 1991	Lo et al.	
☐	5071651	December 1991	Sabara et al.	
☐	5238823	August 1993	Potter et al.	
☐	5273889	December 1993	Potter et al.	
☐	5403586	April 1995	Russell-Jones et al.	
☐	5422110	June 1995	Potter et al.	
☐	5534257	July 1996	Mastica et al.	
☐	5543312	August 1996	Mellors et al.	
☐	5547657	August 1996	Potter	
☐	5594107	January 1997	Potter et al.	
☐	5708155	January 1998	Potter et al.	
☐	5723129	March 1998	Potter et al.	

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2099707	March 1994	CA	
WO 86/07383	December 1986	WO	
WO 90/11298	October 1990	WO	
WO 91/02799	March 1991	WO	
WO 91/15237	October 1991	WO	
WO 92/03558	March 1992	WO	
WO 92/19746	November 1992	WO	
WO 93/08290	April 1993	WO	
WO 93/21323	October 1993	WO	
WO 96/24675	August 1996	WO	

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ART-UNIT: 165

PRIMARY-EXAMINER: Minnifield; Nita

ATTY-AGENT-FIRM: Robins and Associates

ABSTRACT:

New immunological carrier systems, DNA encoding the same, and the use of these systems, are disclosed. The carrier systems include chimeric proteins which include a leukotoxin polypeptide fused to one or more selected GnRH multimers which comprise at least one repeating GnRH decapeptide sequence, or at least one repeating unit of a sequence corresponding to at least one epitope of a selected GnRH molecule. Under the invention, the selected GnRH sequences may all be the same, or may correspond to different derivatives, analogues, variants or epitopes of GnRH so long as the GnRH sequences are capable of eliciting an immune response. The leukotoxin functions to increase the immunogenicity of the GnRH multimers fused thereto.

4 Claims, 15 Drawing figures

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L2: Entry 2 of 2 File: USPT Feb 8, 2000

US-PAT-NO: 6022960
DOCUMENT-IDENTIFIER: US 6022960 A

TITLE: GnRH-leukotoxin chimeras

DATE-ISSUED: February 8, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Potter; Andrew A.	Saskatoon			CA
Manns; John G.	Saskatoon			CA

US-CL-CURRENT: 536/23.1; 424/184.1, 424/235.1, 435/252.3, 435/320.1, 435/69.3, 435/69.7, 536/23.4, 536/23.7

CLAIMS:

We claim:

1. A DNA construct encoding a chimeric protein, wherein the chimeric protein comprises:

the amino acid sequence depicted in FIGS. 9A through 9F (SEQ ID NO:15 and SEQ ID NO:16).

2. An expression cassette comprised of:

(a) the DNA construct of claim 1; and

(b) control sequences that direct the transcription of said construct whereby said construct can be transcribed and translated in a host cell.

3. A host cell transformed with the expression cassette of claim 2.

4. A method of producing a recombinant polypeptide comprising:

(a) providing a population of host cells according to claim 3; and

(b) culturing said population of cells under conditions whereby the polypeptide encoded by said expression cassette is expressed.

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L3: Entry 2 of 2 File: USPT Oct 19, 1999

US-PAT-NO: 5969126
DOCUMENT-IDENTIFIER: US 5969126 A

TITLE: GNRH-leukotoxin chimeras

DATE-ISSUED: October 19, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Potter; Andrew A.	Saskatoon			CA
Manns; John G.	Saskatoon			CA

ASSIGNEE-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY	TYPE CODE
University of Saskatchewan	Saskatoon			CA	03

APPL-NO: 08/ 878748 [PALM]
DATE FILED: June 19, 1997

PARENT-CASE:
CROSS-REFERENCE TO RELATED APPLICATION This application is a divisional of U.S. patent application Ser. No. 08/387,156, filed Feb. 10, 1995, now U.S. Pat. No. 5,723,127, which is a continuation-in-part of application Ser. No. 07/960,932 filed on Oct. 14, 1992 (now U.S. Pat. No. 5,422,110), which is a continuation-in-part of application Ser. No. 07/779,171 filed on Oct. 16, 1991 (now abandoned).

INT-CL: [06] C07 H 2/04, C07 H 2/02, C12 P 21/06, A61 K 39/02

US-CL-ISSUED: 536/23.5; 536/23.4, 536/23.7, 435/69.1, 435/69.3, 435/69.7, 435/172.1, 435/172.3
US-CL-CURRENT: 536/23.5; 435/252.31, 435/252.33, 435/254.21, 435/69.1, 435/69.3, 435/69.7, 536/23.4, 536/23.7

FIELD-OF-SEARCH: 536/23.4, 536/23.7, 536/23.5, 435/69.1, 435/69.3, 435/69.7, 435/172.1, 435/172.3

PRIOR-ART-DISCLOSED:

U.S. PATENT DOCUMENTS

Search Selected | Search ALL

	PAT-NO	ISSUE-DATE	PATENTEE-NAME	US-CL
☐	4556555	December 1985	Esbenshade	
☐	4608251	August 1986	Mia	
☐	4975420	December 1990	Silversides et al.	
☐	5028423	July 1991	Prickett	
☐	5055400	October 1991	Lo et al.	
☐	5071651	December 1991	Sabara et al.	
☐	5238832	August 1993	Potter et al.	
☐	5273889	December 1993	Potter et al.	
☐	5422110	June 1995	Potter et al.	
☐	5476657	December 1995	Potter	
☐	5594107	January 1997	Potter et al.	
☐	5708155	January 1998	Potter et al.	
☐	5723129	March 1998	Potter et al.	

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FOREIGN-PAT-NO	PUBN-DATE	COUNTRY	US-CL
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2099707	March 1994	CA	
PCT/US86/01226	December 1986	WO	
WO 90/11298	October 1990	WO	
WO 91/02799	March 1991	WO	
WO 91/15237	October 1991	WO	
WO 92/03558	March 1992	WO	
WO 92/19746	November 1992	WO	
WO 93/08290	April 1993	WO	

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Adams, T.E., et al., "Feedlot Performance of Steers and Bulls Actively Immunized Against Gonadotropin-Releasing Hormone" J. Anim. Sci. (1992) 70:1691-1698.
Arimura, A., et al., "Production of Antiserum to LH-Releasing Hormone (LH-RH) Associated with Gonadel Atrophy in Rabbits: Development of Radioimmunoassays for LH-RH" Endocrinology (1973) 93(5):1092-1103.
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ART-UNIT: 165

PRIMARY-EXAMINER: Minnifield; Nita

ATTY-AGENT-FIRM: Robins & Associates

ABSTRACT:

New immunological carrier systems, DNA encoding the same, and the use of these systems, are disclosed. The carrier systems include chimeric proteins which comprise a leukotoxin polypeptide fused to a selected GnRH multimer which consists essentially of at least one repeating GnRH decapeptide sequence, or at least one repeating unit of a sequence corresponding to at least one epitope of a selected GnRH molecule. Under the invention, the selected GnRH sequences may all be the same, or may correspond to different derivatives, analogues, variants or epitopes of GnRH so long as the GnRH sequences are capable of eliciting an immune response. The leukotoxin functions to increase the immunogenicity of the GnRH multimer fused thereto.

21 Claims, 8 Drawing figures

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L3: Entry 2 of 2 File: USPT Oct 19, 1999

US-PAT-NO: 5969126
DOCUMENT-IDENTIFIER: US 5969126 A

TITLE: GNRH-leukotoxin chimeras

DATE-ISSUED: October 19, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Potter; Andrew A.	Saskatoon			CA
Manns; John G.	Saskatoon			CA

US-CL-CURRENT: 536/23.5; 435/252.31, 435/252.33, 435/254.21, 435/69.1, 435/69.3, 435/69.7, 536/23.4, 536/23.7

CLAIMS:

We claim:

1. A DNA construct encoding a chimeric protein comprising a leukotoxin polypeptide fused to a multimer having more than one selected gonadotropin releasing hormone (GnRH) polypeptide, said DNA construct comprising a first nucleotide sequence encoding a leukotoxin polypeptide operably linked to a second nucleotide sequence encoding a GnRH multimer.

2. The DNA construct of claim 1 comprising the nucleotide sequence depicted at nucleotide positions 31-2931, inclusive, of SEQ ID NO:7, or a nucleotide sequence that hybridizes thereto in a Southern hybridization reaction under stringent conditions.

3. The DNA construct of claim 1 comprising the nucleotide sequence depicted at nucleotide positions 31-1632, inclusive, of SEQ ID NO:9, or a nucleotide sequence that hybridizes thereto in a Southern hybridization reaction under stringent conditions.

4. A DNA construct encoding a chimeric protein, wherein the chimeric protein comprises a leukotoxin polypeptide fused to first and second multimers wherein the C-terminus of the first multimer is fused to the N-terminus of the leukotoxin polypeptide and the N-terminus of the second multimer is fused to the C-terminus of the leukotoxin polypeptide, and further wherein each of said multimers comprises more than one selected gonadotropin releasing hormone (GnRH) polypeptide, said DNA construct comprising:

a first nucleotide sequence encoding the first GnRH multimer; and

a second nucleotide sequence encoding the second GnRH multimer;

wherein said first and second nucleotide sequences are operably linked by a third nucleotide sequence encoding a leukotoxin polypeptide.

5. An expression cassette comprised of:

(a) the DNA construct of claim 2; and

(b) control sequences that direct the transcription said construct whereby said construct can be transcribed and translated in a host cell.

6. An expression cassette comprised of:

(a) the DNA construct of claim 3; and

(b) control sequences that direct the transcription said construct whereby said construct can be transcribed and translated in a host cell.

7. An isolated host cell transformed with the expression cassette of claim 4.

8. An isolated host cell transformed with the expression cassette of claim 5.

9. An isolated host cell transformed with the expression cassette of claim 6.

10. A method of producing a recombinant polypeptide comprising:

(a) providing a population of host cells according to claim 7; and

(b) culturing said population of cells under conditions whereby the polypeptide encoded by said expression cassette is expressed.

11. A method of producing a recombinant polypeptide comprising:

(a) providing a population of cells according to claim 8; and

(b) culturing said population of cells under conditions whereby the polypeptide encoded by said expression cassette is expressed.

12. A DNA construct encoding a chimeric protein comprising a leukotoxin polypeptide fused to a multimer having eight selected gonadotropin releasing hormone (GnRH) polypeptides, wherein the C-terminus of the leukotoxin polypeptide is fused to the N-terminus of the multimer.

13. The DNA construct of claim 12, wherein the leukotoxin polypeptide comprises the 52 kD LKT 111 carrier polypeptide, as depicted at amino acid positions 11-491, inclusive, of SEQ ID NO:10.

14. A DNA construct encoding a chimeric protein comprising a leukotoxin polypeptide fused to a multimer having eight selected gonadotropin releasing hormone (GnRH) polypeptides, wherein the C-terminus of the multimer is fused to the N-terminus of the leukotoxin polypeptide.

15. The DNA construct of claim 14, wherein the leukotoxin polypeptide comprises the 52 kD LKT 111 carrier polypeptide, as depicted at amino acid positions 11-491, inclusive, of SEQ ID NO:10.

16. An expression cassette comprised of:

(a) the DNA construct of claim 12; and

(b) control sequences that direct the transcription of said construct whereby said construct can be transcribed and translated in a host cell.

17. An expression cassette comprised of:

(a) the DNA construct of claim 14; and

(b) control sequences that direct the transcription said construct whereby said construct can be transcribed and translated in a host cell.

18. An isolated host cell transformed with the expression cassette of claim 16.

19. An isolated host cell transformed with the expression cassette of claim 17.

20. A method of producing a recombinant polypeptide comprising:

(a) providing a population of host cells according to claim 18; and

(b) culturing said population of cells under conditions whereby the polypeptide encoded by said expression cassette is expressed.

21. A method of producing a recombinant polypeptide comprising:

(a) providing a population of host cells according to claim 19; and

(b) culturing said population of cells under conditions whereby the polypeptide encoded by said expression cassette is expressed.

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L4: Entry 7 of 7 File: USPT Nov 17, 1998

US-PAT-NO: 5837268
DOCUMENT-IDENTIFIER: US 5837268 A

TITLE: GnRH-leukotoxin chimeras

DATE-ISSUED: November 17, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Potter; Andrew A.	Saskatoon			CA
Manns; John G.	Saskatoon			CA

ASSIGNEE-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY	TYPE CODE
University of Saskatchewan	Saskatoon			CA	03

APPL-NO: 08/ 694865 [PALM]
DATE FILED: August 9, 1996

PARENT-CASE:
CROSS-REFERENCE TO RELATED APPLICATION This application is a continuation-in-part of U.S. patent application Ser. No. 08/387,156, filed 10 Feb. 1995, U.S. Pat. No. 5,723,129, which is a continuation-in-part of U.S. patent application Ser. No. 07/960,932, filed 14 Oct. 1992 (issued as U.S. Pat. No. 5,422,110), which is a continuation-in-part of U.S. patent application Ser. No. 07/779,171, filed 16 Oct. 1991, abandoned, which applications are incorporated by reference herein in their entireties and from which priority is claimed pursuant to 35 USC .sctn.120.

INT-CL: [06] A61 K 38/00, A61 K 39/02, C12 N 15/00, C07 K 2/00

US-CL-ISSUED: 424/255.1; 424/184.1, 424/200.1, 424/198.1, 424/193.1, 424/192.1, 530/300, 530/350, 514/2, 514/7, 514/12 , 514/15, 935/11, 935/12, 935/13
US-CL-CURRENT: 424/255.1; 424/184.1, 424/192.1, 424/193.1, 424/198.1, 424/200.1, 514/12, 514/15, 514/2, 514/7, 530/300, 530/350

FIELD-OF-SEARCH: 424/184.1, 424/200.1, 424/198.1, 424/255.1, 424/193.1, 424/192.1, 530/300, 530/350, 514/2, 514/7, 514/12, 514/15, 935/11, 935/12, 935/13

PRIOR-ART-DISCLOSED:

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☐	5476657	December 1995	Potter	
☐	5534257	July 1996	Mastico et al.	
☐	5543312	August 1996	Mellors et al.	
☐	5594107	January 1997	Potter et al.	
☐	5708155	January 1998	Potter et al.	
☐	5723129	March 1998	Pottter et al.	

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9203558	March 1992	WO	
WO 92/19746	November 1992	WO	
WO 93/08290	April 1993	WO	
WO 93/21323	October 1993	WO	
WO 96/24675	August 1996	WO	

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ART-UNIT: 165

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ABSTRACT:

New immunological carrier systems, DNA encoding the same, and the use of these systems, are disclosed. The carrier systems include chimeric proteins which include a leukotoxin polypeptide fused to one or more selected GnRH multimers which comprise at least one repeating GnRH decapeptide sequence, or at least one repeating unit of a sequence corresponding to at least one epitope of a selected GnRH molecule. Under the invention, the selected GnRH sequences may all be the same, or may correspond to different derivatives, analogues, variants or epitopes of GnRH so long as the GnRH sequences are capable of eliciting an immune response. The leukotoxin functions to increase the immunogenicity of the GnRH multimers fused thereto.

23 Claims, 42 Drawing figures

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TITLE: GnRH-leukotoxin chimeras

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INVENTOR-INFORMATION:

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CLAIMS:

We claim:

1. A chimeric protein comprising a leukotoxin polypeptide fused to first and second multimers, wherein the C-terminus of the first multimer is fused to the N-terminus of the leukotoxin polypeptide and the N-terminus of the second multimer is fused to the C-terminus of the leukotoxin polypeptide, and further wherein each of said multimers comprises more than one selected GnRH polypeptide.

2. The chimeric protein of claim 1 wherein the first and second GnRH multimers are different and comprise molecules according to the general formula [GnRH-X-GnRH].sub.n, wherein:

GnRH comprises a GnRH polypeptide;

X is selected from the group consisting of a peptide linkage, an amino acid spacer group and a leukotoxin polypeptide; and

n is an integer greater than or equal to 1.

3. The chimeric protein of claim 1 wherein the first and second GnRH multimers are the same and comprise molecules according to the general formula [GnRH-X-GnRH].sub.n, wherein:

GnRH comprises a GnRH polypeptide;

X is selected from the group consisting of a peptide linkage, an amino acid spacer group and a leukotoxin polypeptide; and

n is an integer greater than or equal to 1.

4. The chimeric protein of claim 3 wherein X is an amino acid spacer group having at least one helper T-cell epitope.

5. The chimeric protein of claim 3 wherein n is 4.

6. The chimeric protein of claim 1 wherein the leukotoxin polypeptide lacks cytotoxic activity.

7. The chimeric protein of claim 6 wherein the leukotoxin polypeptide is the polypeptide depicted at amino acid residues 11-923 of SEQ ID NO:6.

8. The chimeric protein of claim 6 wherein the leukotoxin polypeptide is the polypeptide depicted at amino acid residues 11-491 of SEQ ID NO:10.

9. The chimeric protein of claim 6 wherein the leukotoxin polypeptide is SEQ ID NO:17.

10. The chimeric protein of claim 3 wherein the first multimer further comprises the amino acid sequence (Met-Ala-Thr-Val-Ile-Asp-Arg-Ser SEQ ID NO:21) fused to the N-terminus thereof.

11. The chimeric protein of claim 1 comprising the amino acid sequence depicted in FIGS. 9-1 through 9-6 (SEQ ID NO:15 and SEQ ID NO:16).

12. A vaccine composition comprising the chimeric protein of claim 1 and a pharmaceutically acceptable vehicle.

13. A vaccine composition comprising the chimeric protein of claim 3 and a pharmaceutically acceptable vehicle.

14. A vaccine composition comprising the chimeric protein of claim 5 and a pharmaceutically acceptable vehicle.

15. A vaccine composition comprising the chimeric protein of claim 6 and a pharmaceutically acceptable vehicle.

16. A vaccine composition comprising the chimeric protein of claim 11 and a pharmaceutically acceptable vehicle.

17. A method for presenting selected GnRH multimers to a subject comprising administering to said subject an effective amount of the vaccine composition according to claim 12.

18. A method for presenting selected GnRH multimers to a subject comprising administering to said subject an effective amount of the vaccine composition according to claim 13.

19. A method for presenting selected GnRH multimers to a subject comprising administering to said subject an effective amount of the vaccine composition according to claim 14.

20. A method for presenting selected GnRH multimers to a subject comprising administering to said subject an effective amount of the vaccine composition according to claim 15.

21. A method for presenting selected GnRH multimers to a subject comprising administering to said subject an effective amount of the vaccine composition according to claim 16.

22. A method for reducing the incidence of mammary tumors in a mammalian subject comprising administering a therapeutically effective amount of the vaccine composition of claim 12 to said subject.

23. A method for reducing the incidence of mammary tumors in a mammalian subject comprising administering a therapeutically effective amount of the vaccine composition of claim 16 to said subject.